Remarks

Rejection under 35 U.S.C. § 112, second paragraph:

Claim 1 is rejected for lack of clarity under 35 U.S.C. § 112, second paragraph, on the basis that the provisos is unclear. Claim 1 has been amended to overcome this rejection.

Rejection under 35 U.S.C. § 103(a):

Claim 1 is rejected as obvious under 35 U.S.C. § 103(a) over European Patent Application '145. Applicant traverses this basis for rejection. The proviso of Claim 1 has been amended to enhance its clarity. This amendment also clarifies the patentable distinction between Claim 1 and the cited compounds of European Patent Application '145. According to the amended proviso of claim 1 of the present application, R_1 can be neither hydrogen nor carbobenzyloxy-, if R_3 is hydroxyl. The cited compounds of European Patent Application '145 fall precisely into this category. Accordingly, Claim 1, as amended, is patentably unobvious over European Patent Application '145.

Rejection under 35 U.S.C. § 102(b):

Claim 23 is rejected as being anticipated by Dreyer et al. under 35 U.S.C. § 102(b). Claim 23 has been cancelled.

Rejection under 35 U.S.C. § 103(a):

Claim 3 is rejected as obvious under 35 U.S.C. § 103(a) over Handa et al. Applicant's amendment to Claim 3 obviates this basis for rejection.

Rejection under 35 U.S.C. § 102(b):

Claim 1 is rejected as being anticipated by Tam et al. under 35 U.S.C. § 102(b). The amendment to Claim 1 clarifying the proviso obviates this basis for rejection.

Rejection under 35 U.S.C. § 102(b):

Claim 1 is rejected as being anticipated by WO Patent Application '100 under 35 U.S.C. § 102(b). The amendment to Claim 1 clarifying the proviso obviates this basis for rejection.

Rejection under 35 U.S.C. § 103(a):

Claims 10, 12-15, and 23 are rejected as being obvious under 35 U.S.C. § 103(a) over WO Patent Application '948. Applicant traverses this rejection with respect to claims 10 and 12-15. Claim 23 has been cancelled. Claims 10 and 12-15 are directed to protease inhibitors of the indicated structure wherein R^1 is a dipeptide, with the P-2 positions of this dipeptide being occupied by valine. The Examiner points out that WO Patent Application '948 discloses similar protease inhibitors wherein, *inter alia*, the P-2 positions are occupied by alanine. More particularly, the Examiner points to compounds 9, 108, and 125 of '948. The Examiner then states that it would have been obvious to a person of ordinary skill in the art to substitute valine for alanine.

Firstly, it should be pointed out that, since compound 23 has been cancelled, compound **125** of '948 is no longer relevant to this basis of rejection.

Compounds **9** and **108** of '948 employ a dipeptide for R^1 with alanine at the P-2 positions. However, '948 does not disclose or suggest that the activity of these protease inhibitors may be enhanced by substituting a valine for alanine at the P-2 positions. '948 reports, at the bottom of page 31, in an activity table, that compound **9** has an inhibitory activity of 0.58 K_i (μM) with respect to rHIV-1 protease. '948 does not disclose the activity of its compound **108**. Compound **9** of '948 corresponds to compound **8** of the present application, except that compound **9** of '948 employs alanines rather than valine at the P-2 positions. In Figure 11 of the present application, Applicant discloses that compound **8** of the present application has an inhibitory activity of 62 K_i (nM) with respect to HIV-1 protease and that this compound also has inhibitory activity with respect to FIV protease. Accordingly, the present application teaches that substitution of valine for alanine at the P-2 positions enhances the activity of the

inhibitor by approximately one order of magnitude. In contrast, '948 does not disclose or suggest any motivation for substituting valine for alanine at the P-2 positions. Accordingly, the compounds of claims 10 and 12-15 of the present application are patentably unobvious over '948.

Rejection under 35 U.S.C. § 102(b):

Claim 23 is rejected as being anticipated by Huff under 35 U.S.C. § 102(b). Claim 23 has been cancelled.

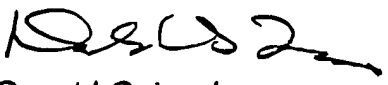
Rejection under 35 U.S.C. § 103(a):

Claim 3 is rejected as being obvious under 35 U.S.C. § 103(a) over Slee et al. Applicant has amended claim 3 so as to obviate this basis of rejection.

Summary:

Claims 6-9 and 19-22 have been allowed. Claims 1, 3, and 6-23 have been rejected. Claims 1 and 3 have been amended and Claim 23 has been cancelled. Applicant believes that Claims 1 and 3, as amended, and Claims 6-22 are novel, patentably clear, and patentably unobvious. Notice of Allowance of amended claims 1, 3, and 6-22 is respectfully requested.

Respectfully submitted,



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APPENDIX

VERSION OF SPECIFICATION AND CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please amend the first two paragraphs following the title of the invention added by amendment on June 19, 2001 as follows:

[International application PCT/US98/25964 was published in English.]

Cross-Reference to Related Application:

The present application claims priority from and is a national stage application under 35 U.S.C. § 371 of copending International Application No. PCT/US98/25964, filed December 8, 1998 and published in English, which claims priority, under 35 U.S.C. § 119(e), from provisional application Serial No. 60/067,959, filed December 8, 1997, the disclosures of which are hereby incorporated by reference.

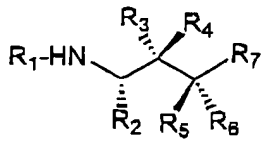
APPENDIX

VERSION OF SPECIFICATION AND CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

A marked-up version of amended claims 1 and 3 showing the changes made are provided below. Claim 23 has been cancelled.

1. (twice amended) A protease inhibitor represented by the following structure:



wherein

R_1 is selected from the group consisting of hydrogen, carbobenzyloxy-, [carbobenzyloxy-valine-,] carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-alanine-asparagine-, carbobenzyloxy-threonine-valine- and carbobenzyloxy-valine-valine-;

R_2 is selected from the group consisting of $-CH_2$-Phenyl, and $-CH_2-CH(CH_3)_2$;

R_3 is selected from the group consisting of hydrogen, oxygen and hydroxyl; R_4 is selected from the group consisting of hydrogen, oxygen and hydroxyl, wherein R_3 and R_4 are not both hydroxyl and wherein R_3 and R_4 are either not oxygen or are a single combined oxygen forming a carbonyl group;

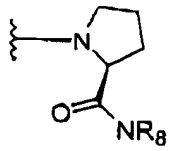
R_5 is selected from the group consisting of hydrogen, and oxygen; R_6 is selected from the group consisting of hydrogen, and oxygen, wherein R_5 and R_6 are either a single combined oxygen forming a carbonyl group or both [seperately]

APPENDIX

VERSION OF SPECIFICATION AND CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

separately hydrogen;

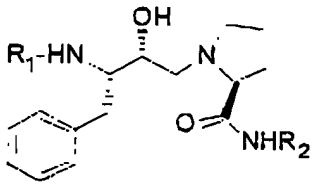
R_7 is a radical represented by the formula:



wherein R_8 is a radical selected from the group consisting of -$(H)_2$, and -H(t-Butyl);

with a proviso that, if either [R_2 or] R_3 or R_4 is hydroxyl, [the] then R_1 is neither hydrogen nor carbobenzyloxy-.

3. (thrice amended) A stereochemically pure protease inhibitor represented by the following structure:

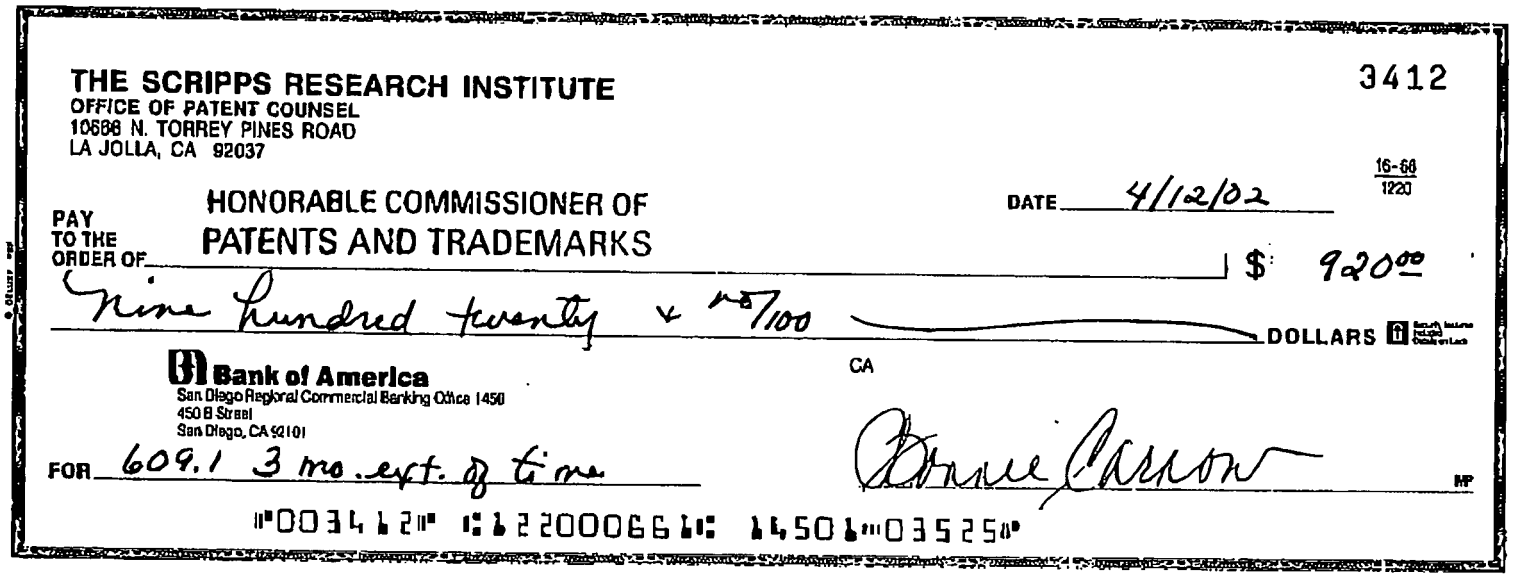


wherein

R_1 is a radical selected from the group consisting of [hydrogen, carbobenzyloxy-, carbobenzyloxy-valine-,] carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-threonine-valine- , carbobenzyloxy-alanine-asparagine- and carbobenzyloxy-valine-valine-; and

R_2 is a radical selected from the group consisting of -$(H)_2$, and -H(t-Butyl).

Please cancel Claim 23 without prejudice.



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OPT 0020P

Applicant (s):	Lee, et al.
Application No.:	09/581,044
Date Filed:	June 8, 2000
Title of Invention:	HIV/FIV PROTEASE INHIBITORS HAVING A SMALL P3 RESIDUE

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- Fee Transmittal (1 page)
- Petition for a 3 Month Extension of Time (1 page)
- Response to Office Action (____ pages)
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